

- 2 -

RECEIVED
CENTRAL FAX CENTER

SEP 28 2006

Commissioner of Patents
USSN 10/661,415REMARKS

Claims 1-38 are pending in the application. Claims 1, 2, 14-32 and 38 are under examination. Claims 3-13 and 33-37 have been withdrawn.

Claim rejections - 35 U.S.C. § 112

Claims 1-2, 14-32 and 38 have been rejected under 35 USC § 112, first paragraph. The Examiner mentioned that the specification and claims do not adequately describe the distinguishing features or attributes concisely shared by the members of the genus comprising oligonucleotides with non-sequence complementary mode of action and comprising random sequences, whereby prevention and treatment of RSV or parainfluenza virus is obtained in a subject. In order to overcome this rejection, Applicants wish to respectfully point out that it is mentioned in the Manual of Patent Examining Procedure that:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the genus" (Manual of Patent Examining Procedure 2163.05).

Further, it is disclosed in the present description that in the case of RSV, Example 5 and corresponding figures 25a-c and 26 disclose various sequences of oligonucleotides with different length (for example REP 2004, 20mer randomer; REP 2006, 40mer randomer; and REP 2007, 80mer randomer) to prove their efficacy as potential anti-RSV molecules. In addition, in the case of parainfluenza virus, Example 8 discloses the efficacy of PS-ODN randomers, for example REP 2006, for the treatment of pediatric bronchiolitics caused by RSV and Parainfluenza-3. The present application is disclosing at least 3 different oligonucleotides, unrelated in term of their sequence and not complementary to any sequence

- 3 -

Commissioner of Patents
USSN 10/661,415

of the targeted RSV and parainfluenza virus. It is thus believed that the present description is disclosing a sufficient and representative number of species. The distinguishing features or attributes concisely shared by the members of the genus claimed in the present application is that the oligonucleotides have an antiviral activity occurring by a non-sequence complementary mode of action. They do not have any other common feature other than not be complementary to any sequence of targeted RSV and parainfluenza virus. Further, the oligonucleotides used in the present invention and claimed in claims 1-2, 14-32 and 38 can be randomer oligonucleotides. As defined on page 14 of the present description, the term "randomer" is intended to mean a single stranded DNA having a wobble (N) at every position, such as NNNNNNNNNN. Each base is synthesized as a wobble such that the randomer oligonucleotides of the present invention actually consist of a population of different randomly generated sequences of the same size. By the nature of the preparation used to produce them, sequence complementary mode of action cannot occur. For example, in a 15 μ mol preparation of a randomer oligonucleotide containing 31 nucleotides in length, this preparation will have at most 2 copies of every possible sequence of nucleotides. Thus, the presence of 2 copies of a specific sequence can not account for the response observed in the present invention. It is believed that a person skilled in the art would acknowledge that disclosure is providing a representative number of species and that the Applicants were in possession of the claimed genus comprising at least 10 or 40 nucleotides in length with antiviral activity occurring principally by a non-sequence complementary mode of action, and which contain randomer oligonucleotides providing treatment and prophylactic effects against RSV or parainfluenza virus infection. In view of the arguments presented hereinabove, reconsideration and withdrawal of Examiner's rejection is earnestly solicited.

Claims 1-2, 14-32 and 38 have been rejected under 35 USC § 112, first paragraph. The Examiner mentioned that the present application contains subject matter which is not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. The Examiner further alleged that the present invention encompasses *in vivo* therapy for treating RSV and parainfluenza virus infection in a patient by administering one or more oligonucleotide. Citing the reference of Shigeta, the Examiner mentioned that the delivery of oligonucleotide, more specifically relating to antisense oligonucleotides, to target sense RNA and the sensitivity of the hybrid to Rnase, *in vivo*, is highly unpredictable.

- 4 -

Commissioner of Patents
USSN 10/661,415

In addition, Examiner cited the Goodman & Gilman's document to argue that *in vitro* assays cannot duplicate the complex conditions of *in vivo* therapy and results in *in vitro* systems may not be reproducible in *in vivo* system. In order to overcome this rejection, Applicants respectfully point out that results are disclosed in the present application demonstrating the antiviral activity of the oligonucleotides claimed in the present application targeting RSV and parainfluenza virus. For example, in the case of RSV, Example 5 and corresponding figures 25a-c and 26 disclose various oligonucleotides with different length used to identify their efficacy as potential anti-RSV molecules. In addition, in the case of parainfluenza virus, Example 8 discloses the efficacy of PS-ODN randomers, for example REP 2006, for the treatment of pediatric bronchiolitis caused by RSV and Parainfluenza-3. In addition, it is believed that the present invention has clinical relevance and that the *in vitro* results disclosed in the present application do not diverge from *in vivo* responses. To support this latter allegation, enclosed is a Declaration of Dr. Jean-Marc Juteau, one of the inventors, reporting *in vivo* results obtained with an *in vivo* models of RSV viral infections (respiratory syncytial virus cotton rat model). This *in vivo* model is widely accepted for testing the activity of compounds *in vivo* (for support, please find enclosed references of Maggon & Barik, 2004, Rev, Med Virol. 14: 149-168; and Sidwell & Barnard, 2006, Antiviral Res. 71: 379-390). From the results reported in this Declaration, it is clear that the teaching contained in the present application is predicative of success for *in vivo* therapy. In view of the foregoing, reconsideration and withdrawal of the Examiner's rejection of claims 1-2, 14-32 and 38 under 35 U.S.C. § 112, first paragraph, are respectfully requested.

Claim rejections - 35 U.S.C. § 102

Claims 1-2, 14-15, 17-32 and 38 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Peyman *et al.* (US Patent No. 6,013,639). The Examiner states that Peyman *et al.* teaches oligonucleotides where the nucleotides sequence is from 10 to 40 nucleotides in length. The oligonucleotides further have phosphorothioate or methyl phosphonate bridges that increase stability of said oligonucleotides. In addition, Peyman teaches complete or partial replacement of the deoxyribose units. The oligonucleotides of Peyman can be linked to molecules which are known to have a favorable influence on the properties of antisense oligonucleotides. Peyman teaches sense nucleotides, as well as antisense. In order to

- 5 -

Commissioner of Patents
USSN 10/661,415

overcome this rejection, Applicants respectfully point out that, contrary to the teaching of the present application, Peyman *et al.* teaches that the efficacy of the tested oligonucleotides is dependent on the presence of a 10 guanines extension at each extremity of the oligonucleotides. It is clearly stated in Peyman *et al.* (column 1 and 2, under the Summary section), that:

"It has now been found that a very simple option exists for significantly improving unmodified or modified oligonucleotides with regards to their nuclease resistance and cell penetration, so that their activity is substantially improved, by extending the oligonucleotides at the 3' end and/or 5' end by from one to 10 guanines.

Surprisingly, the novel oligonucleotide also exhibit a tendency to associate or aggregate. It is possible that they too form G quartet structures by the association of two or more oligonucleotide. Such structures would protect against exonuclease degradation and lead to an increased uptake in cell."(emphasis added)

These oligonucleotides adopt a « G quartet » structure, which is not required in the present invention. The present application neither claims nor teaches that the efficacy of the oligonucleotides claimed is dependent on the presence of a 10 guanines extension at each extremity of the oligonucleotides. On the contrary, there is no such constraint in the sequence of the oligonucleotides claimed in the present invention. Furthermore, Peyman *et al.* never taught or disclosed an oligonucleotide having an antiviral activity occurring by a non-sequence complementary mode of action. In Peyman *et al.*, the modified oligonucleotides need to be directed to a specific target to exhibit activity. The specification of Peyman *et al.* is full of examples of antisense oligonucleotides that are directed to specific targets. See column 6, lines 11-12 and 30-31, column 7, lines 25-28, column 8, lines 29-30, column 10, lines 35-36, column 11, lines 4-5 and column 14, lines 14-15, among others. In fact, Peyman *et al.* only provides for the teaching of modified oligonucleotides for improving nuclease resistance and cell penetration. Peyman *et al.* suggests that the modified oligonucleotides have activity, such as antiviral activity, only if such oligonucleotides target specific viral targets through an antisense mechanism - with a sequence dependent mode of

- 6 -

Commissioner of Patents
USSN 10/661,415

action. Again, nowhere does Peyman *et al.* discloses a method for the prophylaxis or treatment of a RSV or parainfluenza virus infection by administering an oligonucleotide having an antiviral activity occurring by a non-sequence complementary mode of action. In view of the arguments submitted hereinabove, reconsideration of the Examiner's rejections is respectfully requested.

Claim rejections - 35 U.S.C. § 103

Claim 16 has been rejected under 35 U.S.C. § 103(a) as being obvious in view of Peyman *et al.* (US Patent No. 6,013,639). The Examiner mentioned that it would have been obvious to the person skilled in the art to optimize the formulation with the desired concentration for effective antiviral activity. In order to overcome this rejection, Applicants submit that as mentioned previously, Peyman *et al.* teaches that the efficacy of the tested oligonucleotides is dependent on the presence of a 10 guanines extension at each extremity of the oligonucleotides. These oligonucleotides adopt a « G quartet » structure, which is not required in the present invention. The present application neither claims nor teaches that the efficacy of the oligonucleotides claimed is dependent on the presence of a 10 guanines extension at each extremity of the oligonucleotides. In Peyman *et al.*, the modified oligonucleotides need to be directed to a specific target to exhibit activity (see column 6, lines 11-12 and 30-31, column 7, lines 25-28, column 8, lines 29-30, column 10, lines 35-36, column 11, lines 4-5 and column 14, lines 14-15, among others). In fact, Peyman *et al.* only provides for the teaching of modified oligonucleotides for improving nuclease resistance and cell penetration. Peyman *et al.* suggests that the modified oligonucleotides have activity, such as antiviral activity, only if such oligonucleotides target specific viral targets through an antisense mechanism - with a sequence dependent mode of action. Again, nowhere does Peyman *et al.* discloses a method for the prophylaxis or treatment of a RSV or parainfluenza virus infection by administering an oligonucleotide having an antiviral activity occurring by a non-sequence complementary mode of action. Thus, there is no incentive or suggestion in Peyman *et al.*, or any other reference of record, for a person skilled in the art to optimize the formulation with the desired concentration for effective antiviral activity since Peyman *et al.* is not teaching or suggesting a method for the prophylaxis or treatment of a RSV or parainfluenza virus infection by administering an oligonucleotide having an antiviral activity

- 7 -

Commissioner of Patents
USSN 10/661,415

occurring by a non-sequence complementary mode of action. In view of the arguments submitted hereinabove, reconsideration of the Examiner's rejections is respectfully requested.

It is submitted, therefore, that the claims are in condition for allowance. Reconsideration of the Examiner's rejections is respectfully requested. Allowance of claims 1, 2, 14-32 and 38 at an early date is solicited.

No additional fees are believed to be necessitated by this amendment. Should this be in error, authorization is hereby given to charge Deposit Account No. 19-5113 for any underpayment or to credit any overpayment.

- 8 -

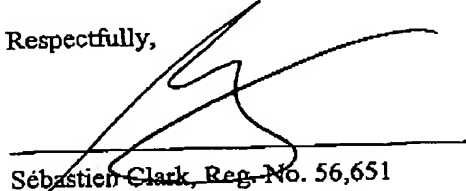
Commissioner of Patents
USSN 10/661,415

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application may be expedited.

Respectfully,

Date: September 28, 2006

By:


Sébastien Clark, Reg. No. 56,651
Agent for Applicants

OGILVY RENAULT
1981 McGill College, Suite 1600
Montreal, Quebec H3A 2Y3
CANADA (514) 847-4256

Enc. -Declaration of Jean-Marc Juteau
-Petition of extension of time
-Dr. Jean-Marc Juteau curriculum vitae
-Documents of Maggon & Barik and Sidwell & Barnard

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted
to the
Patent and Trademark Office on the date shown below.

Sébastien Clark
Name of person signing certification


Signature

September 28, 2006
Date